

18. (New) A synthase according to claim 1, wherein the decarboxylating functionality of the loading module is provided by a ketosynthase-type domain which differs from a KS domain of an extension module by having a glutamine residue in place of cysteine in the active site.
19. (New) A synthase according to claim 1, wherein the decarboxylating functionality of the loading module is provided by a CLF-type domain.
20. (New) A synthase according to claim 1, wherein the loading module's loading functionality is provided by an acyltransferase-type domain having an arginine residue in the active site.
21. (New) A type I polyketide synthase according to claim 20, wherein the acyltransferase domain is a natural extension module acyltransferase domain.
22. (New) A type I polyketide synthase according to claim 1, wherein the loading and decarboxylating functionality is provided by a KS_q-Atq pair derived from a KS-AT pair of domains which naturally occur together in an extension module.
- Sub
C12*

23. (New) A type I polyketide synthase according to claim 20, wherein said acyltransferase domain is specific for loading with malonyl.

24. (New) A type I polyketide synthase according to claim 20, wherein said acyltransferase domain is specific for loading with methylmalonyl.

25. (New) A type I polyketide synthase according to claim 20, wherein said acyltransferase domain is specific for loading with ethylmalonyl.

*See
C19*
26. (New) A type I polyketide synthase according to claim 20, wherein said acyltransferase domain is specific for loading with hydroxymethylmalonyl.

27. (New) A type I polyketide synthase according to claim 20, wherein said acyltransferase domain corresponds to the acyltransferase of module 4 of the FK506 polyketide synthase.

*See
C20*
28. (New) A synthase according to claim 1, wherein the loading module includes an acyl carrier protein.

29. (New) A synthase according to claim 1, wherein at least the KSq domain of said loading module corresponds to the KSq

domain of the loading module of the PKS multienzyme of oleandomycin, spiramycin, niddamycin, methymycin, tylosin or monensin.

30. (New) A type I polyketide synthase according to claim 1, wherein said polyketide synthase is adapted to synthesize a polyketide selected from

- (a) 12- and 16-membered macrolides with acetate starter units
- (b) 12, 14 and 16-membered macrolides with propionate starter units
- (c) variants of rifamycin, avermectin, rapamycin, immunomycin and FK506 with acetate starter units or propionate starter units
- (d) a polyketide wherein the starter unit gave rise to a sidechain selected from allyl and hydroxymethyl.

31. (New) Nucleic acid encoding the PKS multienzyme of claim 1.

32. (New) A vector containing nucleic acid as defined in claim 31.

33. (New) A transformant organism which has been transformed to contain nucleic acid according to claim 31.

34. (New) A process for producing a polyketide which comprises culturing an organism according to claim 33 and optionally recovering the polyketide.
35. (New) A process according to claim 34 for producing a type I polyketide with a desired starter unit with reduced levels of by-products differing in the nature of the starter unit.
36. (New) A process according to claim 34 for producing a variant type I polyketide which differs from the parent polyketide at least in the nature of the starter unit.
37. (New) A method of producing a synthase according to claim 18 including carrying out site-directed mutagenesis of nucleic acid encoding a KS domain of an extension module so that it encodes glutamine in place of cysteine in the active site; and expressing a protein comprising said ketosynthase-type domain in a loading module.
38. (New) A type I polyketide synthase which comprises a loading module and a plurality of extension modules, wherein said loading module is adapted to load an optionally substituted malonyl and then to effect decarboxylation of the loaded residue to provide a corresponding optionally substituted acetyl residue for

transfer to the first extension module, and wherein at least part of the first extension module is heterologous to said loading module or at least a domain thereof; with the proviso that (a) the synthase is not composed of the loading module of the tylosin PKS coupled to the spiramycin PKS minus its natural loading module; and (b) the synthase is not adapted to direct the synthesis of a 14-membered macrolide having a 13-methyl group due to incorporation of an unsubstituted acetate starter unit.

39. (New) A type I polyketide synthase enzyme or part thereof comprising a loading module of the form:

(decarbox) (AT) (ACP) where (ACP) represents an acyl carrier protein

(AT) represents an acyltransferase domain operative to load selectively a substrate selected from optionally substituted malonate units onto the ACP, and

(decarbox) represents a domain operative to decarboxylate an optionally substituted malonate substrate carried by the ACP, the (decarbox) being selected from KSq and CLF-type domains;

wherein the loading module includes domains or portions thereof derived from different sources and/or comprises engineered domains.